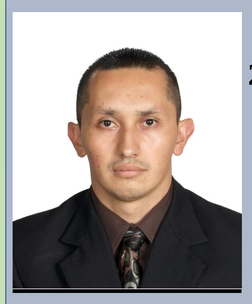
HALOGENATED TYROSINE DERIVATIVES FROM THE PACIFIC ZOANTHARIAN *Antipathozoanthus hickmani*



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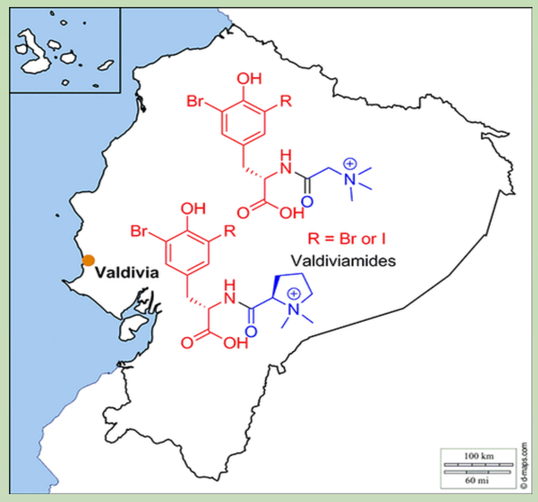
Antipathozoanthus hickmani, a member of the Parazoanthidae family was first described in the Galapagos Islands and recently in the Marine Protected Area El Pelado located at the Peninsula of Santa Elena, Ecuador. It is characterized by its exclusive association with the antipatharian *Antipathes galapaguensis*. During the second chemical study of this zoantharian, four novel halogenated dipeptides named **valdiviamides A-D**, were identified. Valdiviamides A-D are characterized by the presence of bromine and iodine atoms in the phenol ring. The structures were elucidated based on their 1D and 2D NMR experiments and HRESIMS data. The name Valdiviamides were given as a tribute to the Valdivia culture, one of the oldest settled culture in Ecuador and South America.

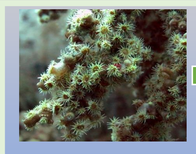


OBJECTIVES

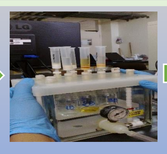
- Investigate deeply the chemical diversity of one of the most representative zoantharians from the Tropical Eastern Pacific.
- Identify potential chemical markers for species of the genus *Antipathozoanthus.*
- Identify novel natural products with biological activities

METHODOLOGY

Chemical Screening


Freeze dried *A. hickmani*

2g sample


Solid Phase Extraction (SPE)


UPLC-DAD-ELSD (Metabolic Profile)


Bioassays of fractions / pure compounds

F1: H_2O
F2: H_2O:MeOH 1:1
F3: H_2O:MeOH 1:3
F4: MeOH
F5: MeOH:DCM 3:1
F6: MeOH:DCM 1:1
F7: DCM

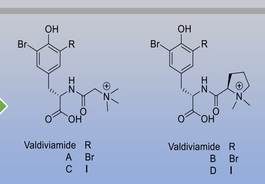
Natural product chemistry


Extraction / VLC


HPLC (Purification)


NMR

HRESI-MS



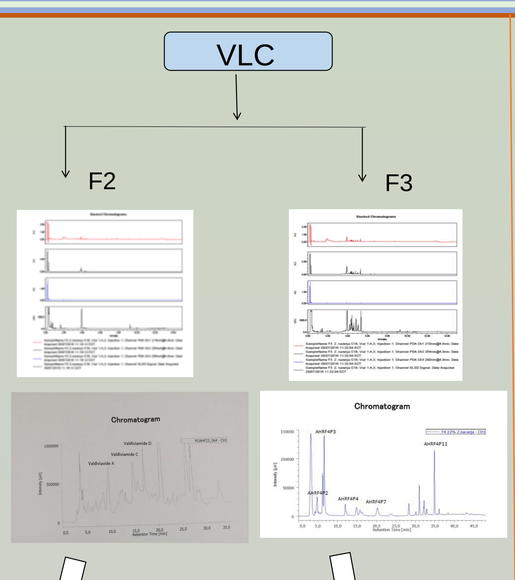
Compounds

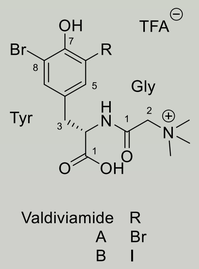
Purification method using a semi-prep HPLC C18 column (SymmetryPrep, 7.8 x 300 mm, 7 µm):

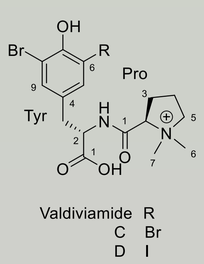
A: H_2O/0.1% TFA

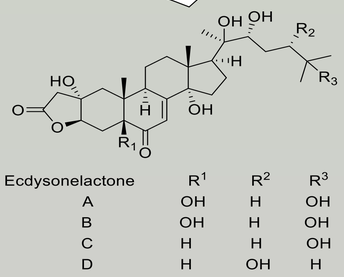
B: CH_3CN/0.1% TFA

0-5 min (95% A/5% B), 5 to 20 min gradient until (65% A, 5% B), 20-30 min isocratic (65% A, 5% B) at a flow rate of 3 ml/min and with UV detection at λ 210 nm.



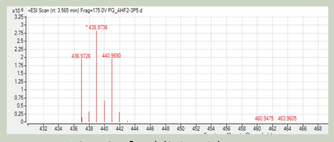


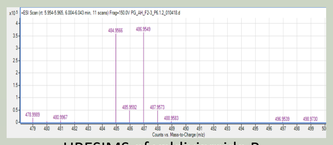


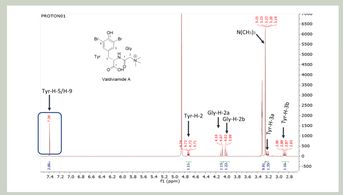


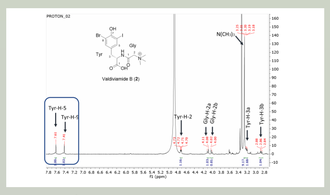
RESULTS

Valdiviamides A-B


HRESIMS of valdiviamide A


HRESIMS of valdiviamide B


^{1}H NMR valdiviamide A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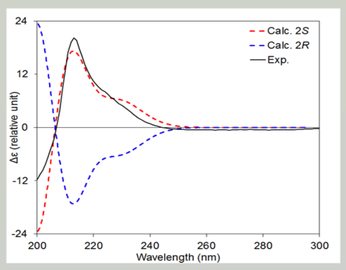
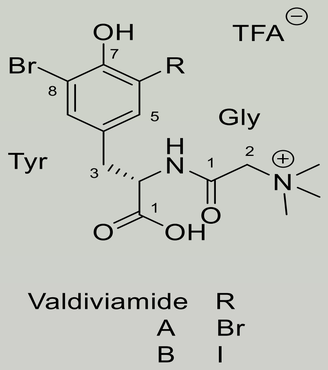
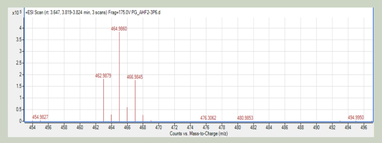
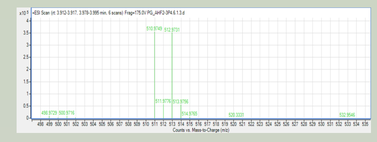


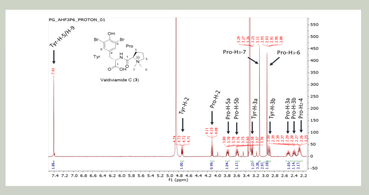
ECD calculation of Valdiviamide A

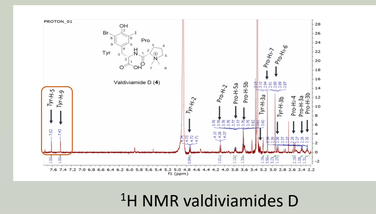


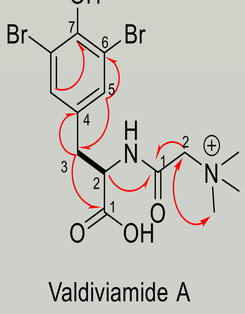
Valdiviamides C-D

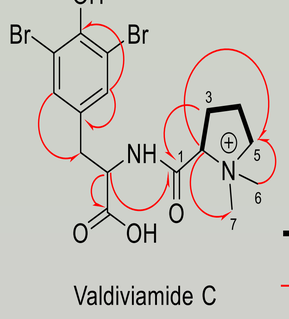

HRESIMS of valdiviamide C


HRESIMS of valdiviamide D

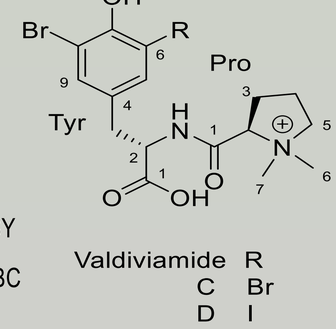

^{1}H NMR valdiviamide C


^{1}H NMR valdiviamides D


Valdiviamide A



Valdiviamide C



DISCUSSION:

- The oceans are the major reservoir in the global iodine cycle. Iodione is present in the seawater as the anions iodine (I^-) and iodate (IO_3^-).
- Tarrant suggested that iodinated organic compounds may affect strobilation and mineralization in cnidarians.
- Among Zoantharians, species of the family Parazoanthidae seems to be capable to concentrate iodine and incorporate into organic compounds (haloperoxidase enzymes)
- Halogenated natural products have exhibited higher biological activity from those of the original compounds (Dembitsky et al., 2005)

CONCLUSIONS:

- Four halogenated dipeptides (valdiviamides A-D) have been identified. These compounds are characterized by the presence of iodine and bromine atoms in the phenol ring.
- The absolute configuration of valdiviamides C-D is proposed to be L-Tyr, D-Pro.
- Valdiviamides A-D represent the first report of halogenated compounds from a specie of the genus *Antipathozoanthus*.
- *A. hickmani* represents an interesting source or novel metabolites, the first chemical studied let to the isolation of four ecdysteroids derivatives named ecdysonelactones A-D characterized by the incorporation of a γ-lactone to the ring A of the ecdysteroids skeleton. Further studies on other species of *Antipathozoanthus* should be carried out to confirm bromotyrosine alkaloids as chemical markers of the family Parazoanthidae.
- Valdiviamide B displayed moderated activity against liver cancer cell line (HepG2) with an IC50 value of 7.8 µM.

ACKNOWLEDGMENTS: To SENESCYT for financially supporting the Marine Biodiversity Project PIC-001. and NUIGalway through the School of Chemistry for the scholarship granted for the PhD Studies.

References: Ann M. Tarrant, Endocrine-like Signaling in Cnidarians: Current Understanding and Implications for Ecophysiology, Integrative and Comparative Biology, Volume 45, Issue 1, January 2005, Pages 201–214; Dembitsky, V. M. (2006) 'Biogenic Iodine and Iodine-Containing Metabolites', Natural Product Communications.